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| EXAMINER | |
|---|---|
| ROBERTS, LEZAH | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/771,388 | ZERBE ET AL. | |
| | Examiner | Art Unit | |
| | Lezah W. Roberts | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *10-31,33-40 and 52-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-31, 33-40 and 52-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is in response to the Request for Continued Examination filed June 5, 2007 and the request by Applicant filed September 6, 2007. All previous rejections have been withdrawn unless stated below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

## *Claims*

**Claim Rejections - 35 USC § 103 – Obviousness (New Rejections)**

1) Claims 10-11, 18-24 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roreger et al. (US 5,456,745).

Roreger et al. disclose hydrophilic gel films that may be used to deliver active substances via the mucous membrane (col. 10, lines 31-35). The films comprise water-soluble polymers such as carboxymethylcelluloses, hydroxyethyl cellulose, hydroxypropyl methylcellulose and karaya gum, which comprise 0.5 to 30% of the films. The films may comprise one or more active substances, which comprises 0 to 50% of the films (col. 1, lines 19-55). The substances include systemic actives such as nicotine (col. 11, lines 20-22) and essential oils such as peppermint (col. 12, line 1). Moisturizers such as glycerol and sorbitol (a sweetener) are included in the films, which comprise 0.1% to 20% of the films. Auxiliaries comprise 0 to 75% of the films. Surfactants such as polyethylene glycol fatty acid ester, polyethylene glycol fatty alcohol ether, or

polyethylene glycol-sorbitan-fatty acid esters and/or softeners, such as glycerol diacetate, which is a surfactant, may be included in the films (col. 3, line 53 to col. 4, line 7). When a softener and a surfactant are used, the combination may be considered two surfactants. Other auxiliaries include thickeners such as polyvinyl pyrrolidone; tackifiers such as natural gums, sugar and honey (col. 7, lines 55-61); penetration accelerators such as fatty acid salts of multivalent metals, betaine and alkyl sulphates; preserving agents such as propylene glycol; and cross-linking agents such as multivalent acids including tartrate and citrate ions. The films are dried to their desired thickness (col. 8, lines 35-40).

The reference differs from the instant claims insofar as it does not disclose an example with all of the components.

It is *prima facie* obviousness to select a known material based on its suitability for its intended use. *See Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945). Also, established precedent holds that it is generally obvious to add known ingredients to known compositions with the expectation of obtaining their known function. See, e.g., *In re Linder*, 457 F.2d 506, 507 (CCPA 1972); see also *In re Dial*, 326 F.2d 430, 432 (CCPA 1964). It would have been obvious to one of ordinary skill in the art to have used the auxiliary agents such as surfactants, softeners, cross-linking agents and tackifiers or mixtures of active agents such as nicotine and peppermint oil in the films of the reference motivated by the desire to obtain their known function such as the surfactants' solubilizing function, the honey's tackifier function (also a sweetener),

the peppermint oil for its therapeutic function (also a flavoring) and nicotine for its therapeutic function as disclosed by the reference and supported by case law.

2) Claims 12-17 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roreger et al. (US 5,456,745) in view of Inoue et al. (US 4,772,470).

The primary reference is discussed above. The reference differs from the instant claims insofar as it does not disclose the thickness of the film or that a coloring agent may be used in the films.

Inoue et al. discloses oral bandages and oral preparations. The preparations comprise an adhesive film comprising a drug. The thickness of the resulting film is preferably adjusted to a range of from 5 to 100 micrometers by controlling the amount of the casting solution, and the like. If a film thickness is less than 5 micrometers it is difficult to obtain sufficient adhesion. A film having a thickness exceeding 100 micrometers tends to produce a feeling foreign to the mouth and to impair softness of the film (col. 8, lines 11-17). Other additives are added to the compositions such as flavoring and coloring matter (col. 10, lines 5-10). The reference differs from the instant claims insofar as it does not disclose nicotine in the compositions.

It would have been obvious to one of ordinary skill in the art to have adjusted the thickness parameters of the films to between 5 to 100 micrometers in the primary reference motivated by the desire to obtain sufficient adhesion while not producing a film that has a foreign feeling in the mouth, as disclosed by the secondary reference.

(Note that this is the same reason preferred by Applicant. See Remarks of the Amendment filed October 16, 2006, page 11, lines 5-6 from the bottom.)

3) Claims 28-29, 31, 33-35, 38-40 and 53-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Lovgren et al. (US 4,786,505) and Inoue et al. (US 4,772,470).

Keith et al. disclose dosage forms for administration of drugs and more particularly buccal dosage forms having a polymeric matrix for controlled release of a drug. The composition comprises three essential ingredients: from about 20% to about 75% by weight of a low molecular weight polyethylene glycol component, from about 2% to about 65% by weight of a medium or high molecular weight polyethylene glycol component, and from about 1% to about 40% by weight of an auxiliary high molecular weight polymer. The dosage forms include disks, wafers, tablets, lozenges, lamellae and the like. Suitable high molecular weight polymers include polyvinylpyrrolidone (PVP), polyethylene oxide (PEO), poly(acrylic acid) (PAA), sodium alginate and carboxymethyl cellulose, which encompasses claim 31. Preferred high molecular weight polymers include polyvinyl pyrrolidone and polyethylene oxide. Both of these polymers provide the matrix with water-activated adhesive properties for good adhesion to the oral mucosa. The polymers are incorporated into the compositions at concentrations ranging fro about 25% to about 40% encompassing claim 33. The dosage form rapidly disintegrates and dissolves after being placed in the mouth, encompassing the instant claims (col. 4, lines 1-20). Additional ingredients may be

incorporated into the buccal matrix of the invention to provide desirable physical properties or modify the properties of the matrix (col. 4, lines 28-33), encompassing claims 34-35. For example, a plasticizer such as propylene glycol may be added in amounts up to about 5% by weight of the matrix. Preferred drugs for incorporation into the buccal dosage form include nicotine (col. 5, line 30). The active ingredient will generally comprise from about 0.01 percent by weight to about 10 percent by weight of the dosage form (col. 5, lines 40-44), encompassing claim 38. Lamellae dosage forms with a certain composition dissolved rapidly when placed in the buccal pouch or sublingually (col. 6, lines 33-35). A small amount of a dye may also be incorporated into the matrix.

The reference differs from the instant claims insofar as the films do not comprise hydroxypropyl methylcellulose and that the thickness of the films is less than 70 micrometers.

Lovegren et al. is used as a general teaching that discloses hydroxypropyl methylcellulose and polyvinyl pyrrolidone are used for rapidly disintegrating compositions. The material for the separating layer is chosen among the pharmaceutically acceptable, water soluble, inert compounds or polymers used for film-coating applications such as, for instance sugar, polyethylene glycol, polyvinylpyrrolidone, polyvinyl alcohol, hydroxypropyl cellulose, methylcellulose, hydroxymethyl cellulose, hydroxypropyl methylcellulose, polyvinyl acetal diethylaminoacetate or the like. The thickness of the layer is not less than 2

micrometers, for small spherical pellets preferably not less than 4 micrometers, for tablets preferably not less than 10 micrometers.

The reference differs from the instant claims insofar as it does not disclose the hydroxypropyl methylcellulose and polyvinyl pyrrolidone in combination with one another or nicotine.

Inoue et al. discloses oral bandages and oral preparations. The reference is used as a general teaching that discloses suitable sizes for films used in the oral cavity. The preparations comprise an adhesive film comprising a drug. The thickness of the resulting film is preferably adjusted to a range of from 5 to 100 micrometers by controlling the amount of the casting solution, and the like. If a film thickness is less than 5 micrometers it is difficult to obtain sufficient adhesion. A film having a thickness exceeding 100 micrometers tends to produce a feeling foreign to the mouth and to impair softness of the film (col. 8, lines 11-17). Other additives are added to the compositions such as flavoring and coloring matter (col. 10, lines 5-10).

The reference differs from the instant claims insofar as it does not disclose nicotine in the compositions.

It would have been obvious to one of ordinary skill in the art to have used hydroxypropylmethyl cellulose as a high molecular polymer used in the compositions of the primary reference motivated by the desire to use a polymer that will not impede the dissolution of the film when placed in the mouth and is used in rapidly dissolving layers, as disclosed by the secondary reference.

It would have been obvious to one of ordinary skill in the art to have adjusted the thickness parameters of the films to between 5 to 100 micrometers in the primary reference motivated by the desire to obtain sufficient adhesion while not producing a film that has a foreign feeling in the mouth, as disclosed by the Inoue et al.

4) Claims 30 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Lovgren et al. (US 4,786,505) and Inoue et al. (US 4,772,470) as applied to claims 28-29, 31, 33-35, 38-40 and 53-56 above, and further in view of Stanley et al. (US 5,783,207).

Keith et al., Lovgren et al., and Inoue et al. are disclosed above. The teachings of the combined references differ from the instant claims insofar as they do not disclose nicotine to be nicotine salicylate.

Stanley et al. disclose dosage forms comprising nicotine and its salts. Nicotine is released from a dosage form and absorbed through the intra-oral mucosal surfaces as the nicotine-containing matrix releases nicotine within the user's mouth. Nicotine is available in either the free base or salt form. Nicotine base is readily absorbed through mucosal membranes but is highly volatile. Nicotine salts, on the other hand, are not readily absorbable through mucosal membranes but are much more stable. Pharmaceutically acceptable nicotine salts include, but are not limited to nicotine hydrochloride and nicotine salicylate. In an alkaline environment, i.e., pH above about 7, and in the presence of an aqueous medium, such as saliva within the oral cavity, nicotine salts react to form nicotine base (col. 7, lines 38-60). In addition to

nicotine in a releasable form, which is readily absorbed transmucosally; the nicotine-containing compositions in accord with the present invention may contain other ingredients such as flavorings, sweeteners, flavor enhancers, lubricants, binders and fillers.

The reference differs from the instant claims insofar as it does not disclose the matrices comprise polyvinyl pyrrolidone and hydroxypropylmethyl cellulose and rapidly disintegrate or soften immediately.

It would have been obvious to one of ordinary skill in the art to have used the nicotine salts and other ingredients in the compositions of the combined references of Keith et al., Lovgren et al., and Inoue et al. motivated by the desire to produce a dosage form that comprises a nicotine active ingredient that can form the nicotine base when introduced into the oral cavity in the presence of saliva, as disclosed by Stanley et al.

5) Claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Lovgren et al. (US 4,786,505) and Inoue et al. (US 4,772,470) as applied to claims 28-29, 31, 33-35, 38-40 and 53-56 above, and further in view of Story et al. (US 4,944,949).

Keith et al., Lovgren et al., and Inoue et al. are disclosed above. The references differs from the instant claims insofar as they do not disclose incorporating surfactants into the oral compositions.

Story et al. is used as a general teaching to disclose surfactants are used to dissolve drugs. The surfactant is used to dissolve the drug. Surfactants can be

variously classified, and often by reference to the nature of the hydrophilic region, which can be anionic, cationic, zwitterionic or nonionic. The preferred surfactants of the reference are nonionic surfactants, which include polyoxyethylated surfactants, including polyoxyethylated glycol monoethers, polyoxyethylated fatty acids, polyoxyethylated sorbitan fatty esters, and polyoxyethylated castor oils. However, other nonionic surfactants are also particularly appropriate, including sorbitan fatty acid esters, poloxamers, polyethylene glycol fatty acid esters and polyethoxylated glyceryl fatty acid esters. Whatever the precise chemical structure of the surfactant or surfactants used, it is generally preferred to use one or more of those that have been already cleared for human ingestion. Therefore, surfactants with a low toxicity are preferred. One factor affecting the choice of surfactant or surfactants to be used is the hydrophilic-lipophilic balance (HLB), which gives a numerical indication of the relative affinity of the surfactant for aqueous and non-aqueous systems. There may be cases where a mixture of two or more surfactants provides an improved degree of solubilization over either surfactant used alone. Additional components may be added to the compositions such as preservatives, sweeteners and flavoring agents.

The reference differs from the instant claims insofar as it does not disclose the oral compositions as a monolayer film or the oral compositions comprising water-soluble polymers comprising nicotine.

It would have been obvious to one of ordinary skill in the art to have used the surfactants and mixtures thereof in the compositions of the primary reference motivated

by the desire to ensure the drug was thoroughly dissolved and made a uniform mixture throughout the film as taught by the Story et al.

Claims 10-31, 33-40 and 52-56 are rejected.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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